REMARKS

Reconsideration of the rejections set forth in the Office Action mailed May 3, 2006, is respectfully requested in view of the above amendments and the following remarks. By the above amendment, claims 27-30 have been amended, claims 34-37 have been canceled and new claims 40-44 have been added. Support for the above amendments may be found throughout the specification as originally filed. For example, support for reverse transcription polymerase chain reactions can be found at page 38, line 29 to page 39, line 8. Support for new claims 40-44 can be found at page 33, lines 8-10; page 38, lines 6-7; page 11, lines 15-27, and elsewhere throughout the specification as originally filed. The above amendments are not to be construed as acquiescence to the Examiner's stated grounds for rejection and are made without prejudice to prosecution of any subject matter removed or modified by this amendment in a related divisional, continuation or continuation-in-part application.

Claim Rejections Under 35 U.S.C. § 112, First Paragraph (Written Description)

Claims 34-37 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. According to the Examiner, the steps recited in the claimed methods are supported in the context of methods of determining the presence of presence of cancer, but not in the context of methods for monitoring the progression of prostate cancer.

Applicants respectfully traverse this rejection and submit that a skilled artisan, in view of the instant disclosure, would understand and appreciate that the claimed methods of monitoring the progression of prostate cancer were well described, and in Applicants' possession, at the time the application was originally filed. However, in an effort to advance prosecution, Applicants have canceled claims 34-37 at this time in favor of remaining claims 27-30 and new claims 40-44. Withdrawal of this rejection is requested.

Claims 27-30 and 34-37 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. According to the Examiner, the claims are drawn to methods which rely on the amplification of portions of an expressed polynucleotide that comprises SEQ ID NO: 67, 107, 308 or 311. The Examiner further states that the specification does not describe with any degree of particularity a single

member of the genus of polynucleotide sequences obtained from a PCR process utilizing oligonucleotide primers specific for expressed polynucleotide sequences comprising SEQ ID NO: 67, 107, 308 or 311. The Examiner concludes that, absent a detailed and particular description of a representative number of members of the genus of polynucleotides which are amplified, the skilled artisan could not immediately recognize or distinguish members of the polynucleotides within the claimed methods.

Applicants respectfully traverse this rejection. Applicants acknowledge and agree that the claimed methods can involve amplification of portions of the recited SEQ ID NOs:, however it is unclear to Applicants how this serves as basis for an assertion that the claims lack written description support as a result. Applicants have demonstrated in the specification as filed that the claimed sequences possess prostate cancer-associated expression patterns and, accordingly, that by detecting the level of expression of the claimed sequences in a biological sample, important diagnostic information about the presence of prostate cancer is thereby obtained. As described in the specification, and as would be recognized by the skilled artisan, the manner in which the level of expression of a recited SEQ ID NO: is determined is not critical and can be achieved by essentially any expression detection method known and available in the art. Numerous illustrative examples of expression detection techniques are indeed described in the specification as filed, including reverse transcription polymerase chain reaction and transcription-mediated amplification, and these techniques can rely upon amplification of only a portion of an expressed target sequence of interest, while still providing an accurate measure of the level of expression of the target sequence. In this respect, whether the manner in which expression levels are determined relies upon detection or amplification of a portion of an expressed sequence or on detection or amplification of the full length expressed sequence is inconsequential.

As for the Examiner's assertion that the specification lacks a description of a representative number of species of the sequences that would be amplified according to the claimed methods, Applicants submit that this is not required when the nature of the sequences being amplified would be well understood by a skilled individual in view of the steps recited in the claims. Reverse transcription polymerase chain reactions employ two primers that are

specific for a cDNA sequence that has been reverse transcribed from a target mRNA of interest and, upon amplifying product using those primers, what is being amplified is a portion of the cDNA sequence having 5' and 3' ends defined by the positions on the target cDNA sequence to which those primers specifically bind. Accordingly, it is not necessary in this instance to "describe a representative number of members of the genus of polynucleotides which are amplified" when it would be well understood that what is being amplified according to the methods is sequence corresponding to the recited cDNA sequence itself. Nevertheless, in the interest of advancing prosecution of this application but without prejudice to further prosecution in a related application, claims 27-30 have been amended to clarify that what is being detected in the methods is an amplified product corresponding to a polynucleotide of a recited SEQ ID NO:, which amplifies in the presence of the oligonucleotide primers that are specific for that recited SEQ ID NO:. Reconsideration is respectfully requested.

Claim Rejections Under 35 U.S.C. § 112, First Paragraph (Enablement)

Claims 27-30 and 34-37 remain rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. According to the Examiner, Applicants' disclosure has not sufficiently provided parameters, which define or characterize the oligonucleotides necessary to practice the claimed invention, such as the structure, size and sequence of the primers. In addition, according to the Examiner, the claimed methods encompass any and all nucleotide fragments capable of binding to Applicants' target sequences, thereby not precluding fragments which are not prostate-specific. The Examiner also states that the specification has not provided sufficient guidance as to which regions of the target sequences are specific to diagnosing prostate cancer and to which the oligonucleotides must hybridize.

Applicants respectfully traverse this rejection. Methods for carrying out polymerase chain reactions, including the design, synthesis and use of sequence-specific oligonucleotide primers, are routine, well known and firmly established in the area to which this invention pertains. In addition, the specification offers illustrative guidance in this regard concerning the design and use of oligonucleotide primers in the context of the claimed invention (*e.g.*, p. 38, lines 17-28). Further still, the region of a target cDNA sequence to which a pair of

sequence-specific primers binds is not critical, provided they are specific for that target sequence and capable of amplifying the desired product. As long as the primers are specific for the target sequence and effective for amplifying the desired product, the specific position where the primers bind and/or what portion of the target cDNA sequence is amplified is of little consequence, and this would be appreciated by the skilled artisan. Accordingly, to assert that Applicants have not enabled the present claims for lack of sufficient teaching regarding parameters such as the structure, size and sequence of oligonucleotide primers used in the claimed methods is unfounded and improperly belies the level of skill and knowledge in the art. A skilled artisan could, in fact, readily and routinely make sequence-specific oligonucleotide primers and successfully use them in a reverse transcription polymerase chain reaction, as claimed, without any undue experimentation.

Regarding the Examiner's concern that claimed methods encompass any and all nucleotide fragments capable of binding to Applicants' target sequences, thereby not precluding fragments which are not prostate-specific, Applicants respectfully disagree. The claimed methods are clear in requiring that the reaction employs two oligonucleotide primers that are specific for a recited sequence and, in addition, that the two oligonucleotide primers specific for the recited sequence are also effective for amplifying a product in a reverse transcription polymerase chain reaction. Accordingly, the skilled artisan would understand what is being amplified using those primers based on their required specificity for the claimed sequences, and could carry out those amplifications without difficulty using routine techniques. As noted above, claims 27-30 have been amended, for purposes of clarity and to advance prosecution, to specify that what is being amplified in the reverse transcription polymerase chain reaction is a polynucleotide of the recited SEQ ID NOs:.

Reconsideration is respectfully requested.

Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 27-30 and 34-37 also stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. According to the Examiner, the claims involve implementing at least two oligonucleotides in a PCR reaction wherein the primers are specific for an expressed polynucleotide sequence that comprises SEQ ID NO: 67, 107, 308 or 311.

However, the Examiner states that "(i)t seems as if while one primer is specific for the said sequence it is not clear what the other primer is specific for." The Examiner concludes that the metes and bounds cannot be determined.

Applicants respectfully traverse this rejection. The claims require a step of contacting a biological sample obtained from the patient with at least two oligonucleotide primers in a polymerase chain reaction, wherein said oligonucleotide primers are specific for an expressed polynucleotide sequence that comprises a recited SEQ ID NO:. The claims thus require that both oligonucleotides are specific for a sequence comprising the recited SEQ ID NO:. In this respect, Applicants are confused as to the Examiner's comments regarding the specificity of the second primer and request reconsideration and/or clarification on this point.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Applicants respectfully submit that all of the claims remaining in the application are now believed to be in condition for allowance. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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